REMARKS

I. Status of the Claims

Claims 38-42, 48, and 61-66 are pending. No amendments are made herein.

II. Withdrawn Rejections

Applicant acknowledges with appreciation the Examiner's withdrawal in part of several prior rejections based on the cancellation of claims in Applicant's response filed July 17, 2006. *See* Final Office Action at 2. The Examiner has also maintained these rejections in part. Applicant addresses below these maintained rejections along with new rejections asserted by the Examiner in the final Office Action.

III. Rejections Under 35 U.S.C. § 112

A. First Paragraph: Amendment of claim 38 does not add new matter.

In the Final Office Action, the Examiner maintains his rejection of claims 38, 40-42, 48, and 65 under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) . . . had possession of the claimed invention." *Id.* at 3. According to the Examiner, claim 38 recites "a sole active component consisting of at least one 1-hydroxy-2-pyridone of formula I . . . in free form or as a pharmaceutically acceptable salt." *Id.*, emphasis in original. The Examiner, however, states that he cannot find support for a "pharmaceutically acceptable salt" because the specification allegedly states that "when using the compounds in salt form, the adjustment of the pH . . . has to be carried out using organic acids." *Id.* Referring to Lange, the Examiner also suggests that "organic acids, including lactic acid, are known to possess anti microbial action." *Id.* Based on these alleged facts, the Examiner

concludes that Applicant "[has] not shown where support for . . . compounds that contain[s] '1-hydroxy-2-pyridone of formula I salt + non active organic acids' can be found." *Id.* Applicant respectfully traverses for reasons of record and for the following additional reasons.

The Examiner has considered Applicant's previous argument that lactic acid was not an active ingredient in the treatment of seborrheic dermatitis, but that it was used as a pH adjuster, and refers to this argument as "arguments of counsel" that "cannot take the place of evidence in the record." *Id.* at 4. Applicant contends that the Examiner himself has cited to "facts" on the record to support Applicant's statement. In particular, on p.3 of the Final Office Action, the Examiner points to the teaching in the present specification that "when using the compounds in salt form, the adjustment of the pH . . . has to be carried out using organic acids." However, rather than support the Examiner's position that the acid is acting as an antimicrobial, this teaching clearly describes the use of an acid solely for purposes of pH adjustment. In view of this failing alone, the Examiner has unjustly dismissed Applicant's argument.

Moreover, Applicant previously argued that the Examiner has not demonstrated that lactic acid would be active in the treatment of seborrheic dermatitis. The Examiner now responds by citing Lange for the alleged teaching that "acids *per se* possess an antimicrobial action." *Id.* at 5. Thus, the Examiner concludes, "an acid like lactic acid 'per se' enhances 'antimycotic' action . . . " *Id.* Referring to information obtained from Wikipedia, the Examiner suggests that such antimycotic action "would include the treatment of seborrheic dermatitis because it is caused by the yeast *Malassezia furfur* (formerly known as *Pityrosporum ovale*)." *Id.*

In making the rejection under 35 U.S.C. §112, first paragraph, the Examiner is pulling one sentence from Lange (regarding the antimicrobial action of acids) and using it to support his position while ignoring the rest of the reference's teachings. Lange as a whole describes the use of a two composition system to treat dandruff. The first composition, "phase I," is a detergent composition with a pH preferably in the neutral or weakly alkaline range. Lange at 6. The second composition, "phase II," "contains a solution of physiologically acceptable organic acid or mixture of these acids" and does not contain detergents. *Id.* at 3, second paragraph, and at 9, third paragraph. In discussing these two compositions, a detergent-containing shampoo and an acid-containing rinse, Lange clearly instructs that "soaps are not well suited for making lower pH products. . . Thus, the *simultaneous action of the two previously mentioned compositions included in one shampoo is practically not feasible*." Id. at 4, second full paragraph, emphasis added.

Therefore, Lange's invention requires the use of two separate compositions, packed separately ". . . because *both compositions may not be mixed without loss of effectivity* . . . and because the synergistic effect of the components used in both liquids is only obtained if they are used one directly after the other!" *Id.* at 11, last paragraph, emphasis added. In other words, Lange teaches that when the acid is mixed with a detergent-containing solution, any alleged antimycotic effect is destroyed. The composition described in present claim 38 comprises "at least one surfactant chosen from anionic surfactants, cationic surfactants, nonionic surfactants, and amphoteric surfactants." Lange's phase I composition similarly contains "various anionic, kationic [sic], non-ionic or amphoteric detergents." Based on Lange's teaching that the

surfactant composition I must be kept separate from the acid composition II, it does not make sense to conclude that an organic acid, when added to such a surfactant composition, would retain its alleged antimycotic activity, i.e., would still behave as an active ingredient.

In sum, when the presently claimed compounds are used in the claimed composition in salt form, the pH of the composition has to be adjusted using organic acids. But this is not a teaching of a composition with two active ingredients. Rather, the specification's teaching is consistent with a composition in which the "sole active component . . . is a 1-hydroxy-2-pyridone of formula I or a pharmaceutically acceptable salt thereof." The organic acid is not an active ingredient in the sense the Examiner implies, i.e., for treating seborrheic dermatitis. Instead, it is used only in an amount sufficient to adjust the pH of the claimed composition when necessary. When the claims are read in light of the present specification, it is clear that the claimed composition comprises only one active ingredient for treating seborrheic dermatitis.

Because no new matter has been added by Applicant's prior amendment to claim 38, Applicant requests that this rejection be withdrawn.

B. Second Paragraph: Claims 38-42, 48, and 61 are definite.

1. "Pharmaceutically acceptable salt"

The Examiner continues to reject claims 38-42, 48, and 61-66 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. According to the Examiner, the "pharmaceutically acceptable salt" embodiment "requires two active ingredients, (1) the salt of a compound of formula I and (2) the organic acid that is used to adjust the pH." Final Office Action at 6. In light of this interpretation, it is not clear to the Examiner "how

the composition comprises a 'sole' active ingredient[s] when more than one active ingredient[s are] is being claimed." *Id.* Applicant traverses for reasons of record and for the following additional reasons.

As discussed in section III A above, the Examiner's interpretation of Lange is not accurate because the Examiner has not considered the entirety of this reference's teaching. In discussing its two compositions, a detergent-containing shampoo and an acid-containing rinse, Lange clearly instructs, as noted above, that they cannot be used simultaneously, and must be packed separately or lose their effectiveness.

In other words, Lange teaches the use of both compositions, detergent and acid, to treat dandruff. Lange has found a synergistic effect of the components, which is only obtained if they are used one after the other and not simultaneously. If the treatment is not carried out this way, the alleged antimycotic effect of the acid is destroyed. Yet, without the acid, Lange's invention is not complete.

In contrast, the present invention relates to a one-composition treatment (for seborrheic dermatitis, not dandruff, but this point is separately discussed below). This single composition has "a sole active component, which is a 1-hydroxy-2-pyridone of formula I or a pharmaceutically acceptable salt thereof." It does not need an acid to complete its task of treating seborrheic dermatitis. An acid may be employed, as noted, to adjust pH, but this is not the addition of another active ingredient, and no confusion about the metes and bounds of the claims should exist. Accordingly, the claims are definite, and this rejection cannot stand.

2. "Seborrheic dermatitis"

Claims 38-42, 48, 53, 55-59, and 61-67 remain rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite because the term "seborrheic dermatitis" is allegedly unclear in light of the prosecution history. The Examiner correctly quotes Applicant as having said on the record that "Dascalu et al misuses dermatology nomenclature by confusing 'dandruff' with 'seborrheic dermatitis' . . . it is well understood that seborrheic dermatitis is a condition distinct from dandruff." Final Office Action at 6, citing Response filed April 24, 2002. As also noted by the Examiner, "seborrheic dermatitis" is defined in the present specification as a "disorder of the scalp which differs from simple dandruff by the presence of erythema as a sign of inflammation, by the greater degree of scaling with occasional itching and burning, and by the occurrence of eczematous changes to other body sites." *Id.* at 7, citing specification at 1. The specification, as the Examiner points out, also states that "Pityrosporum . . . is assumed to be the cause of seborrheic dermatitis." *Id.*

Despite all of these facts, the Examiner goes on to suggest that Dascalu et al. (WO 96/29045; "Dascalu") teaches the treatment of the "same exact symptoms as defined in Applicant's specification" and "that their treatment inhibits the exact yeast, Pityrosporum." *Id.* Thus, the Examiner concludes, "it is not clear what symptoms, underlying causative agents and/or other physiochemical factors Applicants are relying on to make this distinction." *Id.* Applicant disagrees and contends that the record is consistent in its instruction that dandruff and seborrheic dermatitis are two separate conditions, and further that seborrheic dermatitis as discussed in the specification and the prosecution history is distinguishable from dandruff as described in Dascalu.

As the Examiner notes, the present specification explains that seborrheic dermatitis is a condition of the scalp that differs from simple dandruff in that it is characterized by erythema, a greater degree of scaling with a greater degree of itching and burning, and by the occurrence of eczematous changes in other body sites. Specification, at 1, lines 3-11. Over the course of prosecution in this case, Applicant has submitted a series of declarations designed to further describe seborrheic dermatitis. The declaration of Dr. R. Todd Plott, dated July 17, 2006, was submitted in an Information Disclosure Statement in the present case on September 22, 2006. Dr. Plott, who is a board certified dermatologist and one of ordinary skill in the art, explains in his declaration that "dermatologists know that seborrheic dermatitis is an inflammatory disorder associated with the hyperproliferation of keratinocytes, while dandruff is a 'noninflammatory' scaling of the scalp. While both disorders can include flaking skin among their symptoms, they are known by dermatologists to be different disorders." Plott Declaration at 2. Likewise, Dr. James Leyden, who is a practicing dermatologist and one of ordinary skill in the art, instructs in his declaration dated January 4, 2006, originally filed in related co-pending application no. 10/606,229 and submitted in an Information Disclosure Statement in the present case on September 22, 2006, that seborrheic dermatitis is a "disorder characterized by the hyperproliferation of keratinocytes in the skin. It is characterized by erythema (redness of the skin), scaling and yellow crusted patches. . . . Essentially, in seborrheic dermatitis, the epidermal keratinocytes multiply too quickly, causing scaling and other symptoms." Leyden declaration at 2.

Finally, Applicant submitted a declaration by Dr. Mitchell S. Wortzman on June 9, 2003, during appeal of the present case. Dr. Wortzman has a Ph.D. in cellular and molecular biology and has been involved in research and development for numerous dermatological products. Dr. Wortzman's declaration, dated June 6, 2003, explains that "dandruff is a 'noninflammatory' scaling of the scalp, while 'seborrheic dermatitis is an inflammatory erythematous, and scaling eruption that occurs in seborrheic areas . . . such as the scalp, face, and trunk.'" Wortzman declaration at 2. The Wortzman declaration further teaches that "even the scales of dandruff look different from the scale from seborrheic dermatitis; dandruff has thin, white or gray flakes, while seborrheic dermatitis has oily, yellowish scales with inflammation." *Id.*

Each of the above descriptions contributes to a single, consistent description and definition of seborrheic dermatitis. In contrast, Dascalu does not describe the hyperproliferation of keratinocytes or the presence of "crusted patches" on the skin. Also, while Dascalu appears to generally describe scaling of the skin, both dandruff and seborrheic dermatitis can include flaking skin among their symptoms, as noted above. However, Dascalu does not mention the "hyperproliferation of keratinocytes" that is the hallmark of seborrheic dermatitis (as noted by Dr. Leyden), nor does Dascalu teach "oily, yellowish scales," which result from this condition.

Moreover, the present specification explains that the yeast Pityrosporum is "assumed" to be the cause of seborrheic dermatitis. Specification at 1, line 33. The Examiner incorrectly interprets this as teaching that Pityrosporum *does* cause seborrheic dermatitis. With this incorrect interpretation in hand, the Examiner turns to Dascalu, suggesting that "Dascalu . . . explicitly state[s] that their treatment inhibits the

exact yeast, Pityosporum." Final Office Action at 7. The Examiner's reasoning, however, does not necessarily follow. Although the symptoms of seborrheic dermatitis are distinguishable from dandruff, it is unclear what causes seborrheic dermatitis. A hypothesis that "favored an etiology involving bacteria, yeasts, or both ... has remained unsupported." Dermatology in General Medicine, 5th ed., page 2 of 17 (filed as Appendix A of the Wortzman declaration). Some in the art argue that "*P. ovale* is not the causative organism but is merely present in large numbers." *Id.* at page 3 of 17. Other possible causes of seborrheic dermatitis include drugs, neuralgic abnormalities that affect the nervous system, physical factors such as temperature and humidity and nutritional disorders. *Id.* at pages 3-4 of 17. This reference also states that "Imidazoles [e.g. ketoconazole], like other antifungal agents, have a wide spectrum of effects, including anti-inflammatory properties and inhibition of cell wall lipid synthesis. Their efficacy is not proof of a causal relationship between *P. ovale* and seborrheic dermatitis." *Id.* at page 10 of 17. Thus, with the causes of seborrheic dermatitis being unclear, the alleged teaching in Dascalu that its disclosed treatment inhibits Pityrosporum says nothing about the effectiveness of Dascalu's treatment of seborrheic dermatitis.

Finally, the Examiner points to Janniger et al. for allegedly teaching that seborrheic dermatitis "is a common condition that usually appears as simple dandruff." Final Office Action at 9. But as explained in the declarations and in the specification, this comparison is incorrect. As discussed above, Applicant has defined the term "seborrheic dermatitis" as set forth in the specification and declarations, reflecting the understanding of one of ordinary skill in the art.

In sum, both the specification and the prosecution history are clear and definite on the meaning of the term "seborrheic dermatitis." Applicant has explained in detail how the seborrheic dermatitis differs from the condition described in Dascalu. Accordingly, the claims containing the term "seborrheic dermatitis" are definite and Applicant requests that the Examiner withdraw this rejection.

IV. Rejections Under 35 U.S.C. § 102

A. Lagarde teaches a "combination product"

Claims 39 and 61-64 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lagarde "as evidenced by" Wikipedia. Final Office Action at 9. According to the Examiner, Lagarde teaches a "combination product comprising an anti-fungal agent selected from the 1-hydroxy-2-pyridones such as ciclpirox [sic] or octopirox and, secondly, crotamiton as an antifungal agent activity enhancer." *Id.* at 10. Lagarde also allegedly teaches "at least one 1-hydroxyl-2-pyridone of formula I as the sole active component . . . . " and "the use of a surfactant . . . (. . . Cocamide DEA, Cocamide MEA, Cocamidopropyl betaine are disclosed)." *Id.* Acknowledging that Lagarde does not state that Cocamide DEA, Cocamide MEA and Cocamidopropyl betaine are surfactants, the Examiner relies on an entry from Wikipedia to suggest that "these would be inherent properties of these molecules." *Id.* at 11. The Examiner also points to an Internet publication by Green People (http://www.greenpeople.co.uk/Organics_Features_SLS.htm) to allegedly show that sodium lauryl sulphate is an "anion surfactant" that is included in a variety of commonly used products including shampoo. *Id.* Regarding claim 61, Lagarde allegedly discloses the "cyclohexyl R4 group." *Id.* Regarding claim 64, Lagarde allegedly discloses "at

least one 'additional' surfactant such as cocamidopropyl betaine + Cocamide MEA." *Id.* Applicant respectfully traverses for the reasons of record and the following additional reasons.

A claim is anticipated under 35 U.S.C. § 102(b) only if each and every element as set forth in the claim is found in a single reference. *See Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) and M.P.E.P. § 2131. Furthermore, the identical invention must be set forth in as complete detail as it appears in the claim. See *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989) and M.P.E.P. § 2131. Lagarde cannot be said to anticipate the present invention because it does not disclose each and every element of the present claim, even when one takes the internet references into account.

Applicant has previously argued that Lagarde requires his composition to be a "combination product" that benefits from the "synerg[isit]ic association of products [the 1-hydroxy-2-pyridones and crotamiton]." Response dated July 17, 2006, at 10. Lagarde, therefore, fails to teach each and every element of the pending claims. Specifically, Lagarde does not teach non-combination products, i.e., a "single" composition comprising a "sole" active component, or the use of 1-hydroxy-2-pyridones as a sole active component. Instead, Lagarde is entirely focused on the synergism resulting from the combination of his two active ingredients, i.e., the treatment of "skin fungal infections" with a composition comprising ***two separate compounds*** - 1-hydroxy-2-pyridone and crotamiton. In contrast, the method of claim 39 describes administering to the patient a ***single composition*** with a ***sole*** active component.

Regardless of this contrast, the Examiner again suggests in the Final Office Action that Applicant's claims encompass more than just one active ingredient, relying on the same reasoning used to support his rejection under 35 U.S.C. § 112, second paragraph, above. Final Office Action at 11. Applicant disagrees for reasons similar to those set forth above in response to the §112 rejection. Here, Lagarde teaches a synergistic combination of ingredients to treat "skin fungal infections." The present invention, however, relates to a one-composition treatment. This single composition has "a sole active component, which is a 1-hydroxy-2-pyridone of formula I or a pharmaceutically acceptable salt thereof." It does not have a second ingredient such as crotamiton acid to enhance or complete its task of treating seborrheic dermatitis.

Because Lagarde describes a "combination product" with more than one active ingredient, this reference does not and cannot anticipate claims 39 and 61-64. Applicant has also previously pointed out the dangers of relying on Wikipedia as a source of reliable information, noting that anyone may contribute, change, delete, or add an entry at will. The Examiner now responds by suggesting that Wikipedia is "justas [sic] reliable as other more traditionally sources of information like Britannica" and cites a study comparing Wikipedia to Britannica, allegedly concluding that the difference in reliability was "not particularly great." *Id.* at 12 and 13. The Wikipedia is anonymous and unreviewed, while Britannica is signed and reviewed, thereby making it much more reliable. Moreover, the proffered declarations were made under oath and prepared by persons of indisputable credentials, which certainly have more weight than Wikipedia. The rejection is in error and should be withdrawn.

B. Lange teaches two separate compositions

The Examiner rejects claims 39 and 62-64 under 35 U.S.C. § 102(b) as allegedly anticipated by Lange "as evidenced by" Green People (http://www.greenpeople.co.uk/Organics_Features_SLS.htm) and Avre Skin Care (http://www.avro.co.za/misc/about_skincare/cosmetic_ingredients.html). *Id.* The Examiner describes Lange as disclosing "a two phase cleansing, conditioning and medicinal treatment shampoo and methods of use. . . for treating seborrheic dermatitis." *Id.*, emphasis in original. Lange also allegedly teaches that the phase I composition "may contain anti-mycotics in the medicinal as well as the anti-dandruff variant" and that "one may use a water soluble anti-mycotic such as piroctone olamine." *Id.* at 14. The Examiner considers piroctone olamine as falling "within the scope of Applicants' formula I." *Id.* Lange also allegedly teaches sodium lauryl sulphate, which the Examiner contends is inherently an anionic surfactant "as exemplified by Green People" and "at least one 'additional' surfactant such as lauramide DEA," which the Examiner also contends is inherently a surfactant "as exemplified by Aver Skin Care." *Id.* at 15. Applicant disagrees.

As discussed above, independent claim 39 recites administering a ***sole*** active component in a ***single*** composition. In contrast, Lange describes the use of two compositions to treat dandruff: a detergent composition and an acid composition, both needed to achieve Lange's purpose but not usable together simultaneously. The use of these separate compositions in a treatment regime does ***not*** constitute "administering to the patient an amount effective for the treatment of seborrheic dermatitis of a *single composition*" as recited in claim 39.

The Examiner's response to Applicant's prior argument in this regard shows that he has misunderstood not only Applicant's position, but also Applicant's invention. Specifically, the Examiner states that

> a composition that was added "later in time" does not negate the fact that a "single" composition was added first. If this were the case then Applicants' claims would read on situations where patients could never wash their hair again because this "subsequent" application of a composition would qualify as "more than one" composition. * * * If a patient were to apply Applicants' composition in the beginning of the week and then use another shampoo (or medical composition) later in the week . . . then this would have to be regarded . . . as the use of a "second" composition in violation of the current claims requiring a "single" composition.

Final Office Action at 16. The Examiner applies Lange in a way that directly contradicts the teaching of the reference itself. In fact, what Lange discloses is a two-phase shampoo which allows "sequential application of noncompatible substances/conditions." Lange Abstract. Lange treats skin and hair, "especially to control dandruff and similar scale forming conditions," by washing with a detergent composition, rinsing, and then applying the non-detergent acid composition, and "microbial growth is inhibited through both treatments." Lange at 3.

Thus, Lange's method of treatment requires the use of both separate compositions to achieve the touted inhibition of microbial growth. The point here is that a single treatment under Lange's system requires the patient to use ***two separate compositions***. In contrast, the method of claim 39 describes a single treatment that is complete with the use of a ***single composition*** with a sole active component. ***Even if*** an acid is added to the presently claimed composition to adjust pH before use, still only one composition is applied to the hair for treatment of seborrheic dermatitis under the

presently claimed method. The claim term "single composition" cannot be dismissed as lightly as the Examiner tries to do. It is in fact a claim element, and must be present in the cited reference for the rejection under §102 to be proper.

In view of the above, Applicant requests that the Examiner withdraw this rejection under §102(b).

V. Rejection Under 35 U.S.C. § 103

The Examiner maintains his rejection of claims 38-42, 48, and 61-66 as obvious over Lange, FDA (56 FR 63568, Dec. 1991), and Dascalu in view of Green People, Avre Skin Care, Dreumeux (http://www.signus.com/dsoftsoap.htm), Odds (U.S. Pat. 6,514,490), and Brinkster (http://misterguch.brinkster.net/acidtutorial.html). The Examiner applies Lange, Green People, and Aver Skin Care as described in section IV(B) above. Regarding claim 38, the Examiner alleges that Lange "does not teach the use of a pH range between about 4.5 to about 6.5" and "only teaches a 'neutral' pH." Final Office Action at 20. Citing to Dreumeux and Odds, the Examiner contends that "a pH range between 6-8 is generally considered to be neutral for shampoo products." *Id.* Thus, the Examiner concludes, "Lange teaches a pH range that overlaps in scope with the present invention (i.e., pH 6-8 overlaps in scope with a pH of about 4.5 to about 6.5." *Id.* According to the Examiner, where the claimed ranges overlap or lie inside ranges disclosed in the prior art or are close enough that one skilled in the art would expect them to have the same properties, a case of obviousness exists. *Id.* at 21. The skilled artisan would allegedly "expect pirocton olamine to have the same anti-mycotic properties whether it was at a neutral pH (6-8) or more acid pH (4-5). *Id.* The skilled

artisan would allegedly be motivated to adjust the pH to 4-5 using lactic acid because of its "favorable bacterio and mycostatic properties." *Id.* at 22.

The Examiner also notes that Lange and the FDA article "fail to teach the use of a cyclohexyl radical," but the Examiner points to Dascalu for this alleged teaching. *Id.* at 20-22. The Examiner concludes that it would have been obvious to use ciclopiroxolamine in the treatment described in Lange and FDA because Dascalu "explicitly states that ciclopiroxolamine is useful for this purpose." *Id.* at 23. In the Examiner's view, a motivation to make this combination lies in Dascalu's alleged teaching that these compounds are a "preferred embodiment." *Id.* The Examiner also suggests that the skilled artisan would reasonably expect to be successful because Dascalu allegedly teaches "several successful example of using anti-fungal agents like ciclopiroxolamines . . . and it is structurally related to the anti-fungal agents disclosed by the combined references of Lange and FDA." *Id.*

In addition, the Examiner acknowledges that Lange "fails to recite the use of a keratolytic agent. *Id.* at 22. The Examiner believes that it would be obvious to use keratolytic agents "because the FDA explicitly approved this ingredient for its use in treating dandruff and seborrheic dermatitis." *Id.* The skilled artisan would allegedly be motivated to use salicyclic acid with the treatment of Lange because "the FDA states that active ingredients like salicyclic acid are 'recognized as safe and effective'" and have a reasonable expectation of success "because the FDA approved the use [of] keratolytic agents like salicyclic acid for the treatment of dandruff and seborrheic dermatitis and also shows its use with pyrithion zinc, which is . . . disclosed as a preferred embodiment of Lange." *Id.*

Applicant traverses the Examiner's arguments for reasons of record and the additional reasons set forth below.

In its recent decision in *KSR Internat. Co. v. Teleflex Inc.* , the Supreme Court confirmed that the "framework for applying the statutory language of §103" was still based on their landmark decision in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966). *See KSR* at 2 (U.S. Apr. 30, 2007)(No. 04-1350). Under *Graham*, there are four factors to be considered when determining whether an invention is obvious:

(1) the scope and content of the prior art;

(2) differences between the prior art and the claims at issue;

(3) level of ordinary skill in the art; and

(4) secondary considerations.

In the following arguments, Applicant has applied these factors to the references cited by the Examiner in light of the Supreme Court's most recent guidance on obviousness as provided in *KSR*. The scope and content of the prior art have been explored at length throughout this response. The differences between the prior art and the present claims are discussed with respect to §102 above and §103 below, and the declarations reflecting the understanding those of ordinary skill in the art have been offered. Finally, secondary considerations such as long-felt need and commercial success are part of the record already and are mentioned again below. In Applicants' view, the end result of all of this analysis is that the Examiner has not made a prima facie case of obviousness even in light of the *KSR* decision.

The teachings of the prior art differ from the claims at issue in that none of the several references relied on by the Examiner when taken alone or in combination teach

treating seborrheic dermatitis by administering a single composition, wherein this composition comprises a sole active component which is a 1-hydroxy-2-pyridone of formula I or a pharmaceutically acceptable salt thereof. As discussed above in section IV(B), the Examiner's central reference, Lange, does not teach the use of a single composition for treatment. The Examiner tries to interpret Lange that way, but such an interpretation is not commensurate with what Lange discloses. Although it is true that one of Lange's two compositions (Phase I) may comprise a 1-hydroxy-2-pyridone, Lange clearly teaches the use of two separate compositions to form a single treatment, whereas rejected independent claims 38 and 39 describe the use of a single composition in a single treatment. In other words, Lange does not envision his invention as complete (i.e., dandruff as treated) until both compositions have been used, so it would not have been obvious to one of ordinary skill in the art to use, in effect, only half of Lange's invention (the 1-hydroxy-2-pyridone), and expect good results in treating seborrheic dermatitis, which, as discussed above, is not the same medical condition as dandruff.

As for the secondary references, Dascalu discusses compositions for use in treating dandruff, which is different from seborrheic dermatitis, as discussed above. The Examiner questions whether Applicant relies on the declarations by Dr. R. Todd Plott and Dr. Mitchell S. Wortzman. Final Office Action at 27. As discussed in section III(B)(2) above, Applicant does rely on these declarations to show that dandruff and seborrheic dermatitis are not the same. Indeed, the differences between dandruff and seborrheic dermatitis are significant. Seborrheic dermatitis involves the hyperproliferation of epidermal keratinocytes that results in the formation of reddened,

irritated skin (erythema) and thick oily yellowish scales. The type of scaling associated with seborrheic dermatitis is different from scaling that occurs with dandruff and it is improper for the Examiner to assert that seborrheic dermatitis is present simply because scaling was noted in the reference.

Clearly, as the declarations by Drs. Wortzman, Plott, and Leyden attest, those of ordinary skill in the art consider these conditions to be very different from one another, each with its own etiology. The skilled artisan would not, based on what is generally known about these different conditions, associate a treatment for dandruff with a treatment for seborrheic dermatitis. The Green People and Avre Skin Care references merely provide generic background information on certain chemical agents such as sodium laurel sulphate and lauramide DEA. These references have no link to a method of treating seborrheic dermatitis. Additionally, Applicant reiterates that one of ordinary skill in the art would not typically use these websites. Brinkster and Dreumex appear to provide general background information on the pH scale and the pH of Dreumex soap in particular. Again, neither of these references has anything to do with a method for treating seborrheic dermatitis. Odds, like Lagarde and Lange, teaches a combination product, emphasizing the importance of using both components together rather than alone. Odds at col. 2, lines 32-35. In contrast to the art cited by the Examiner, the rejected claims recite a method of treating seborrheic dermatitis using a single composition comprising as a sole active component a 1-hydroxy-2-pyridone.

Thus, three of the references cited by the Examiner relate to combination products. This is not surprising, given Lange's teaching on the difficulty of preparing a soap with an acid pH. Specifically, Lange explains that "it has been found that soaps

are not well suited for making lower pH products." Lange at page 4. This is why Lange developed a two-composition treatment because "simultaneous action of the two . . . compositions included in one shampoo is practically not feasable." *Id.* The fact that two other references cited by the Examiner also teach combination products reflects an absence in the art of a single composition to treat dandruff (and nothing teaching seborrheic dermatitis). Thus, the references cited by the Examiner clearly teach away from a composition having a sole active ingredient. This secondary consideration, as described in *Graham*, demonstrates the non-obviousness of the rejected claims.

Finally, the FDA reference provides a list of active ingredients for use in treating seborrheic dermatitis. None of these ingredients are 1-hydroxy-2-pyridones, let alone 1-hydroxy-2-pyridones used as a sole active component. The Examiner's suggested combination of Lange and the FDA reference does not result in the presently claimed invention. In fact, the FDA reference does not even teach 1-hydroxy-2-pyridones or a method of treating seborrheic dermatitis while Lange teaches, indeed requires, the use of two compositions. Even if combined, the teachings of these two references, in addition to the general propensity in the art to use multiple-composition treatments, would not result in the claimed invention.

The Examiner interprets the information provided in the declaration by Kevin Kriel too narrowly by suggesting that this declaration only speaks to the commercial success of ciclopirox. Final Office Action at 27. Page 2 of this declaration states that "it is clear that treatment of seborrheic dermatitis with a 1-hydroxy-2-pyridone (e.g. ciclopirox) composition with no additional additives, a pH between about 4.5 and 6.5, and a surfactant is really desired by patients and physicians." The statements made in Mr.

Kriel's declaration acknowledge the commercial success of compositions comprising 1-hydroxy-2-pyridone with the claim limitations, using ciclopirox and Loprox® Shampoo as an example. Thus, Mr. Kriel's declaration regarding the commercial success of Loprox® Shampoo demonstrates that claims 38-42, 48, and 61-66 are not obvious.

Therefore, for all of these reasons, the §103 rejection should be removed.

VI. New Rejection Under 35 U.S.C. §102(b)/ §103

The Examiner newly rejects claims 38-42, 48, and 61-66 under 35 U.S.C. § 102(a) as allegedly anticipated by or, in the alternative, under 35 U.S.C. §103(a) as allegedly obvious over Verdicchio (EP 0117135 A2) in view of in view of Janniger and Dittmar (U.S. 4,185,106). *Id.* at 30.

According to the Examiner, Verducchio discloses "a composition for treating dandruff in a human patient," but "do[es] not explicitly state that these people have seborrheic dermatitis." *Id.*. Relying on Janniger, the Examiner suggests that treatment of seborrheic dermatitis "is inherently disclosed because dandruff is a form of Seborrheic Dermatitis." *Id.* Verdicchio's composition allegedly "comprises a sole active component which is hydroxy pyridone such as Octopirox," which "falls within the scope of Applicants' formula I." *Id.* at 30 and 31. The Examiner also suggests that Verdicchio discloses "a pH of 'about' and wherein the composition has pH ranging from about to about 4.5 to 6.5." Id. at 31. Applicant respectfully traverses.

A. Verdicchio does not teach a method of treating seborrheic dermatitis

Verdicchio does not teach a method of treating seborrheic dermatitis. Rather, Verdicchio consistently discusses treating dandruff, which is a separate condition from seborrheic dermatitis, as discussed by Applicant in section III(B)(2) above. Thus,

Verdicchio does not inherently teach a method of treating seborrheic dermatitis and as a result does not teach each and every element of claims 38-42, 48, and 61-66. The Examiner's reliance on Janniger is misplaced, because Janniger improperly confuses the term "dandruff" with the term "seborrheic dermatitis." Accordingly, the rejection over Verdicchio under §102(b) cannot stand and should be withdrawn.

B. Verdicchio does not suggest a method of treating seborrheic dermatitis

With respect to §103, The Examiner applies Verdicchio and Janniger as described above and reasons that the rejected claims would have been obvious "because both dandruff and seborrheic dermatitis are produced by the same causative agent, Pityrosporum ovale, and is generally treated using the same types of medicinal shampoo (e.g., see Janniger et al. . . . " *Id.* at 32 and 33. Thus, the Examiner concludes, "it would be prima facie obvious to treat the 'separate' seborrheic dermatitis condition with dandruff shampoo like the dandruff shampoo set forth in Verdicchio." *Id.* at 33. The skilled artisan would allegedly have had a reasonable expectation of success because, according to the Examiner, both dandruff and seborrheic dermatitis "are produced from a common microbe, Pityrosporum ovale organism." *Id.* The Examiner bases a motivation to combine in the alleged teaching in Dittmar that "pyridones can be used as 'anti-seborrheic' agents.'" *Id.* Applicant disagrees.

1. The Examiner's basis for a reasonable expectation of success is flawed

The Examiner bases a reasonable expectation of success in making the proposed combination of Verdicchio, Janniger, and Dittmar on the perception that dandruff and seborrheic dermatitis are caused by the same organism. But, as Applicant

has explained, it is unclear what causes seborrheic dermatitis. A hypothesis that "favored an etiology involving bacteria, yeasts, or both ... has remained unsupported." Dermatology in General Medicine, 5th ed., page 2 of 17 (filed as Appendix A of the Wortzman declaration). Some in the art argue that "*P. ovale* is not the causative organism but is merely present in large numbers." *Id.* at page 3 of 17. Other possible causes of seborrheic dermatitis include drugs, neuralgic abnormalities that affect the nervous system, physical factors such as temperature and humidity and nutritional disorders. *Id.* at pages 3-4 of 17. Moreover, Lange also instructs that "although yeast cells like Pityrosporum ovale . . . are normally found on the skin, some people do have dandruff while others don't." Lange at 1, third paragraph. This teaching argues against *P. ovale* being the causative agent of dandruff because it is not specifically associated with incidents of dandruff.

Because it is unclear what the causative agent(s) is for the different conditions of dandruff and seborrheic dermatitis, the Examiner's basis for an expectation of success falls. Indeed, as Applicant has explained, there are significant differences between the symptoms of dandruff and seborrheic dermatitis such that one of ordinary skill in the art would not assume a treatment for dandruff could be used for seborrheic dermatitis. For this reason alone, the Examiner has not established a *prima facie* case of obviousness. As a result, this obviousness rejection cannot stand.

2. Anti-seborrheic agents are not anti-seborrheic dermatitis agents

The Examiner cites column 6, line 24 in Dittmar for the alleged teaching that "pyridones can be used as 'anti-seborrheic' agents.'" Dittmar, however, does not teach this. Again, the Examiner has pulled out a part of a sentence and applied it out of

context while ignoring the overall teaching of the reference. Dittmar describes his compositions as compositions that "may be used as an anti-dandruff agent" or "the anti-dandruff compositions according to the invention." See abstract; col. 6, lines 42-47; and col. 7, line 24. As Applicant explained, dandruff is a condition that is different from seborrheic dermatitis and Dittmar's teaching supports this. Applicant notes that the Examiner's FDA reference also lists dandruff and seborrheic dermatitis as separate conditions. Specifically, the citation referred to by the Examiner describes "further additives" that may be added to the anti-dandruff compositions. Dittmar, col. 6, line 12. "Anti-seborrheic agents" are listed as one type of possible additive in Dittmar's anti-dandruff compositions. *Id.* at line 24. As explained on page 1 of chapter 126 of Fitzpatrick (formerly submitted), seborrhea is merely oil. Seborrheic dermatitis is a disorder, as Applicant has noted above several times. Merely dealing with oily skin by using anti-seborrhea agents does not equal treating seborrheic dermatitis.

Moreover, Dittmar's list of further additives teaches away from a method that uses a composition in which 1-hydroxy-2-pyridone is the sole active component of the composition. If anything, a composition with multiple active ingredients is presumably more effective than a composition with just one. None of these references or the Examiner's statements about what is generally known in the art teach the use of a composition in which a 1-hydroxy-2-pyridone is the sole active component. To arrive at such a method, the skilled artisan would have to specifically pick 1-hydroxy-2-pyridone from ingredients such as those listed in Dittmar to arrive at the claimed invention. Making this composition improperly employs hindsight, which the Court in *KSR* confirmed should not be used as a basis for obviousness. *See KSR Internat. Co. v.*

Teleflex Inc. (U.S. Apr. 30, 2007)(No. 04-1350) ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.")

Applicant requests that the Examiner withdraw this rejection.

VI. Obviousness-Type Double Patenting

The Examiner provisionally rejects claims 38-42, 48, and 61-66 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 14-23 and 26-29 of copending application number 10/606,229. Final Office Action at 27. According to the Examiner, the claims in both applications are "drawn to the same treatment of seborrheic dermatitis using the same 1-hydroxy-2-pyridone compounds having the same generic formula. *Id.*

Applicant respectfully traverses this provisional rejection, at least because no actual double-patenting circumstance can arise until a patent issues from the cited application. Since the above copending application is still under consideration, there is the possibility that the claims may change. Applicant further requests that any resolution in the form of submission of a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(c), if necessary, be deferred until such patent issues. Accordingly, Applicant respectfully requests the Examiner to withdraw this provisional rejections of the claims.

Applicant also notes that M.P.E.P. § 804 addresses the situation of two copending applications. The section indicates that "[t]he "provisional" double patenting rejection should continue to be made by the examiner in each application . . . unless that "provisional" double patenting rejection is the only rejection remaining in one of the

applications. In view of the amendments to the claims and remarks on record to obviate the other rejections, applicants submit that the provisional double patenting rejection should be the only remaining rejection. If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent." *See* M.P.E.P. § 804. For at least this additional reason, Applicant requests that any resolution in the form of submission of a Terminal Disclaimer, if necessary, be deferred.

VII. Conclusion

Applicant respectfully requests that this Reply under 37 C.F.R. § 1.113 be entered by the Examiner, placing claims 38-42, 48, and 61-66 in condition for allowance. Because Applicant did not amend the claims, this Reply should allow for immediate action by the Examiner.

Furthermore, Applicant respectfully points out that the final action by the Examiner presented some new arguments as to the application of the art against Applicant's invention. It is respectfully submitted that the entering of the Reply would allow the Applicant to reply to the final rejections and place the application in condition for allowance.

Finally, Applicant submits that the entry of the Reply would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

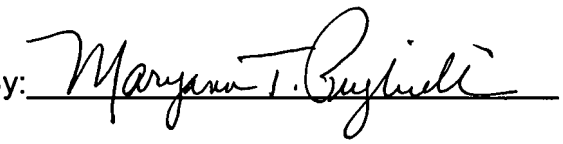
In view of the foregoing remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: June 4, 2007

By: 

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